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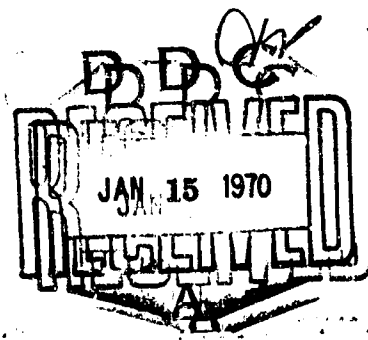
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II. INHIBITION OF MULTIPLICATION OF RIFT VALLEY FEVER VIRUS BY HOMOLOGOUS VIRUS IRRADIATED WITH ULTRAVIOLET RAYS

Comptes Rendus de la Société de Biologie
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In an earlier note¹ we reported the fairly early inhibitory effect of Rift Valley fever virus inactivated by ultraviolet radiation on the multiplication of active homologous virus. In order to determine whether neutralizing antibodies interfere with this inhibition, we performed a series of experiments the results of which are presented below. The materials and procedure were described in the earlier note.

I. After how many hours of neutralizing antibodies would they be detected in animals that received irradiated vaccine? We injected intravenously 5 groups of 8 mice each with 0.4 cm.³ of virus irradiated for 30 seconds. The groups of animals were bled at different intervals. Serum was collected by groups and heated to 56°. These ^{serum specimens} were pooled in equal parts with decimal dilutions of virus in order to evaluate their neutralizing ~~power of the serum specimens~~. Without incubating

¹ I. Sawa, C. R. Soc. Biol., 1955, Vol. 249, p. 2050.

the mixtures we injected fresh mice subcutaneously with 0.25 cm³ of this serum. The results are presented in Table 1. Circulating antibodies were not detected in the vaccinated animals until 4 days after vaccination.

Table 1

Time of Appearance of Neutralizing Antibodies in the Blood
After Vaccination

- 1 - Intervals after vaccination
 - 2 - hours
 - 3 - days
 - 4 - Neutralization index
-

In another experiment, we looked for antibodies in the livers of vaccinated mice. For this purpose we injected the animals intravenously with 0.4 cm³ of irradiated vaccine. The mice were ~~exsanguinated~~ ~~bled~~ after 1 hour, 7 hours, 24 hours, 2 days, 4 days, and 7 days after vaccination. The livers ~~liver by liver,~~ ~~liver by liver,~~ were placed, ~~liver by liver,~~ in a chilled Waring blender with some broth to produce a 10% emulsion. The freezing was repeated 5 times and centrifugation carried out at 3000 rpm for 20

minutes. The supernatant heated to 56⁰ was mixed with virus diluted according to the decimal scale at the rate of 4 to 1. The mice were injected subcutaneously with 0.5 cm³ of each mixture. In the control mixtures, the liver of a vaccinated mouse was replaced with that of a fresh animal. The results are shown in Table II.

Table II

Time of Appearance of Neutralizing Antibodies in the Liver
After Vaccination

1-4 - Same as in Table II

It is evident from the table that neutralizing antibodies were not detected in the liver until day 7 after vaccination. It follows that neutralizing antibodies were not detected in the animal at the time when virus multiplication was inhibited by the vaccine.

II. Would immune serum given after infection inhibit virus multiplication? But if antibodies were present in the animal in a quantity sufficient to inhibit virus multiplication, it would not always reveal, following the usual procedure, taken from the animal. the neutralizing power of the serum. Moreover, it is not certain that antibodies in a detectable quantity given to an animal after infection inhibit virus multiplication.

To clarify these questions, we examined the inhibitory ~~effect~~ ^{effect} of immune serum given in different doses to infected animals.

We inoculated mice with virus in a dose equal to $10^{2.5}$ times the LD₅₀. Three hours after infection we injected them intravenously with 0.4 cm³ of immune serum not diluted or diluted 5- or 10-fold. The immune serum used was the serum taken from rabbits that had been injected subcutaneously with a liver emulsion from infected mice. The undiluted sera and those diluted 10-fold ~~were~~ protected the mice. We titrated the virulence of the liver at different intervals in order to determine whether

the virus multiplies in an animal protected by serum diluted 10-fold. Marked virus multiplication in the liver was observed 15 to 25 hours after infection (Table III). Furthermore, we injected some fresh mice with immune serum diluted 10-fold and exsanguinated them at different intervals. Neutralizing antibodies were readily detected in the blood and liver (Table IV).

Thus, when antiserum is injected into infected animals, the virus multiplies in the presence of antibodies in a detectable quantity.

Table III

Virulence (number of LD₅₀ in log) of the liver in Animals
That Received Immune Serum in Relation to Time

1 - hours

Table IV

Detection of Neutralizing Antibodies in Mice That Received
Immune Serum

1 - Time after injection of immune serum
2 - hour(s)
3 - Neutralization index
4 - blood
5 - liver

Summary

We established the following: (i) The multiplication of Rift Valley fever virus is totally inhibited by an immediate injection of irradiated homologous ~~serum~~^{virus}. (ii) Despite the inhibition, neutralizing antibodies cannot be detected in the animal's body. (iii) Neutralizing antibodies can be found in mice given immune serum for several days after infection. Nevertheless, the virus multiplies to a considerable degree.

The results suggest that neutralizing antibodies do not interfere with the inhibition ~~notes~~ in question.

Intervalles après vaccination	24 heures	48 heures	3 jours	4 jours	5 jours
Indice de neutralisation	0	0	0,3	1,7	2,0

Tableau I. — Moment d'apparition dans le sang d'anticorps neutralisants après vaccination.

Intervalles après vaccination	1 heure	7 heures	24 heures	4 jours	7 jours
Indice de neutralisation	0,15	0,15	0,85	0,85	1,05

Tableau II. — Moment d'apparition dans le foie d'anticorps neutralisants après vaccination.

5 heures	15 heures	25 heures	50 heures	70 heures	90 heures
1,0	4,5	5,0	2,9	2,9	2,5

Tableau III. — Virulence (nombre de DL_{50} en log) du foie chez l'animal ayant reçu de l'immun sérum en fonction du temps.

Temps après l'injection d'immun-sérum	0 heure	1 heure	3 heures	5 heures	15 heures	25 heures	70 heures
> Indice de neutralisation	sang.	5,0		3,7	3,3	3,0	3,7
	foie.	3,35	1,0			1,0	0,7

Tableau IV. — Détection d'anticorps neutralisants chez les souris ayant reçu de l'immun-sérum.